

REMARKS

A Petition for Extension of Time is being concurrently filed with this Amendment. Also, this Amendment is being filed on October 10, 2006, which is a Tuesday after a Federal Holiday (Columbus Day). Thus, this Amendment is being timely filed.

Applicants respectfully request the Examiner to reconsider the present application in view of the foregoing amendments to the claims and present specification and the following remarks.

Status of the Claims

In the present Reply, claims 11, 12, 14, 15 and 17 have been amended. Also, claims 20-29 have been added. Finally, claims 10 and 18 were previously canceled without prejudice or disclaimer of the subject matter contained therein. Thus, claims 1-9, 11-17 and 19-29 are pending in the present application.

No new matter has been added by way of these amendments and new claims because each amendment and new claim is supported by the present specification and/or originally filed claims. For example, the amendments to claims 11, 12, 14, 15 and 17 are for clarification purposes. Further, such amendments are supported throughout the present specification. New claims 20-29 drawn to other embodiments of the present invention have been added for consideration. Support for all of these new claims is found throughout the present specification (see also the discussion below regarding the support for the new claims).

Also, no new matter has been added with the amendments to the present specification, as the amendments reflect the written description as originally filed and/or merely correct typographical errors.

Based upon the above considerations, entry of the present amendment is respectfully requested.

In view of the following remarks, Applicants respectfully request that the Examiner withdraw all rejections and allow the currently pending claims.

Objection to Specification

The specification is objected to as stated in the outstanding Office Action at pages 2-6. Applicants respectfully traverse.

The specification has been amended such that the Examiner's concerns have been adequately addressed. Such changes include deleting any reference to "claims" (see, e.g., paragraph "11." of the original specification at page 7, line 4 which referred to "claims"). Accordingly, this objection has been overcome. Reconsideration and withdrawal of this objection are respectfully requested.

Issues under 35 U.S.C. § 112, Second Paragraph

Claims 11, 12, 14, 15, 16, 17 and 19 stand rejected under 35 U.S.C. § 112, second paragraph, as stated on pages 6-10 of the Office Action. Applicants respectfully traverse.

Applicants respectfully refer the Examiner to the disputed claims as presented herein. The disputed claim language has been clarified. For instance, in claim 11, the value of

expression amount of step (iii) is what was measured in the previous step. Reconsideration and withdrawal of this rejection are respectfully requested.

Issues under 35 U.S.C. § 112, First Paragraph

Claim 19 stands rejected under 35 U.S.C. § 112, first paragraph, for asserted lack of written description (see pages 10-11 of the Office Action).

Also, claims 1-9, 11-17 and 19 stand rejected under 35 U.S.C. § 112, first paragraph, for asserted lack of written description (see pages 12-14 of the Office Action).

Applicants respectfully traverse, and reconsideration and withdrawal of these rejections are respectfully requested.

In the Office Action, the Examiner has emphasized certain genes as not being adequately described. Applicants respectfully traverse the rejection of claims 1-9, 11-17 and 19 as there is proper written description of the full scope of these claims.

First, it is incumbent upon the Patent Office, whenever a rejection on this basis is made, to explain *why* it doubts the truth or accuracy of any statement in a supporting disclosure and to back up assertions of its own with acceptable evidence or reasoning which is inconsistent with the contested statement. *See In re Marzocchi and Horton*, 58 CCPA 1069, 439 F.2d 220, 169 USPQ 367 (CCPA 1971). Second, Applicants note that the primary consideration here is factual and depends on the nature of the invention and the amount of knowledge imparted to those skilled in the art by the disclosure. *In re Wertheim*, 541 F.2d 257, 262, 191 USPQ 90, 96 (CCPA 1976). In this regard, Applicants respectfully submit that the present specification provides detailed information of nucleic acid molecules and cells encompasses by the claims, for example,

regarding ligand-responsive transcription control factors, reporter genes, recognition sequences of ligand-responsive transcription control factors, minimum promoters, selective marker genes, host animal cells and the like. Further, the present specification contains specific examples, accession numbers of sequences identified in public databases, method for obtaining those molecules and cells, etc. Further, and indeed, “[a] patent need not teach, and preferably omits, what is well known in the art.” See *Spectra-Physics, Inc. v. Coherent, Inc.*, 827 F.2d 1524, 1534 (Fed. Cir. 1987). Similarly, a patentee or applicant does not have to recite known DNA structures in the specification, as this “would serve no goal of the written description requirement”. *Falkner v. Inglis*, (2006). Given how much written description is Applicants’ specification, wherein what is omitted in the specification is well known in the art, Applicants respectfully submit that there is ample written description of the disputed claim language.

Accordingly, it is respectfully submitted that this rejection has been overcome. Reconsideration and withdrawal of this rejection are respectfully requested.

Applicants also note claims 20-21 as presented herein. The claims recite a minimum promoter of mouse metallothionein I gene and a chicken ovalbumin gene, respectively.

Issues under 35 U.S.C. § 102(b)

Claims 1, 2, 5, 13, 14 and 17 stand rejected under 35 U.S.C. § 102(b) as being anticipated by Mader and White (U.S. Patent No. 5,512,483; hereinafter referred to as “Mader ‘483”) (see pages 14-16 of the Office Action).

Applicants respectfully submit that the cited Mader ‘483 reference does not disclose all instantly claimed features. A mammalian expression vector as disclosed in Mader ‘483 does not

have any “selective marker gene which can function in [an animal] cell” as instantly claimed. The ampicillin resistance marker contained the expression vector as disclosed in the Mader ‘483 reference (see, e.g., Figure 1 thereof) is a selection marker within bacterial cells. In other words, this marker in Mader ‘483 is not functional in animal cells. Therefore, because “a claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference,” the cited Mader ‘483 reference cannot be a basis for a rejection under § 102(b). *See Verdegaal Bros. v. Union Oil Co. of California*, 814 F.2d 628, 631, 2 USPQ2d 1051, 1053 (Fed. Cir. 1987). Thus, because of the lack of disclosure of all features as instantly claimed, the rejection in view of Mader ‘483 is overcome. Reconsideration and withdrawal are respectfully requested.

Issues under 35 U.S.C. §103(a)

Claims 1, 3-9, 11 and 14-17 stand rejected under 35 U.S.C. § 103(a) as being obvious over Bradfield *et al.* (U.S. Patent No. 5,650,283; hereinafter “Bradfield ‘283”) in view of Waldman *et al.* (*Analytical Biochemistry*, Vol. 258, pp. 216-222 (1998); hereinafter “Waldman”) (see pages 17-21 of the Office Action).

Also, claims 1-9, 11, 12 and 14-17 stand rejected under 35 U.S.C. § 103(a) as being obvious over Bradfield in view of Waldman and in further view of Kushner (U.S. Patent No. 6,117,638; herein “Kushner ‘638”) (see pages 21-23 of the Office Action).

Finally, claims 1, 3-9, 11, 14-17 and 19 stand rejected under 35 U.S.C. § 103(a) as being obvious over Bradfield in view of Waldman and in further view of O’Malley *et al.* (U.S. Patent No. 5,834,213; herein “O’Malley ‘213”) (see pages 23-25 of the Office Action).

Applicants respectfully traverse each of the rejections. Reconsideration and withdrawal of all of these rejections are respectfully requested.

The present invention relates to an animal cell expressing a gene coding a ligand-responsive transcription control factor and stably transformed with a DNA comprising genes (a) and (b) in a molecule, wherein gene (a) is a reporter gene connected downstream from a transcription control region, in which said transcription control region substantially consists of a recognition sequence of said ligand-responsive transcription control factor and a minimum promoter which can function in said cell, and gene (b) is a selective marker gene which can function in said cell. The animal cell is further characterized by the fact that gene (c), which is a reporter gene connected downstream from a promoter which transcription activity is unchanged by having said ligand-responsive transcription control factor contacted with a ligand of said ligand-responsive transcription control factor, said reporter gene (c) coding a protein which can be differentiated from the protein coded by said gene (a), is not present in said cell. Also, the reporter gene (a) is connected downstream from a transcription control region which substantially consists of a recognition sequence of the ligand-responsive transcription control factor and a minimum promoter. In the presently claimed cell, the constitutive background transcription activity is lowered. Since such background activity hinders the measurement of transcription activity, the lowering of such background activity allows for the detection of ligand-responsive transcription activity with higher sensitivity. Also, the Examiner's attention is drawn to claim 19, wherein the minimum promoter is defined as a minimum promoter of a metallothionein I gene or an ovalbumin gene. Such a minimum promoter is a DNA having a

region which determines the transcription initiation site by RNA polymerase II and relates to maintaining a minimum transcription level.

Applicants respectfully submit that the references cited by the Examiner, whether taken alone or in combination, fail to suggest or disclose the presently claimed subject matter. For instance, none of the references discloses an animal cell stably transformed with a DNA comprising in a molecule, a reporter gene (a) connected downstream from a transcription control region which substantially consists of a recognition sequence of the ligand-responsive transcription control factor and a minimum promoter, and a selective marker gene (b). Still, the Examiner has maintained the previous rejections and even cites new references to reject the instant claims.

However, in the present instance, Applicants have pointed out that the cited art, as a whole, fails to suggest or disclose a DNA comprising in a molecule, a reporter gene (a) connected downstream from a transcription control region which substantially consists of a recognition sequence of the ligand-responsive transcription control factor and a minimum promoter, and a selective marker gene (b). In this regard, the teaching or suggestion to make the claimed combination and the reasonable expectation of success must both be found in the prior art, and not based on applicant's disclosure. See *In re Vaeck*, 947 F.2d 488, 20 U.S.P.Q.2d 1438 (Fed. Cir. 1991). That is not the case here. Based upon this deficiency alone, Applicants submit that the Examiner has failed to present a valid *prima facie* case of obviousness for any of the outstanding rejections.

Still, the Examiner says that the claims do not recite the lower background activity/higher sensitivity in the claims (see the paragraph bridging pages 26-27 of the Office Action).

However, such properties are inherent in the present invention and do not need to be recited. Still, Applicants respectfully request the Examiner to consider newly added claims 20-29 as discussed in more detail below. In this regard, Applicants note that in *In re Wertheim*, the court stated: "Inventions are constantly made which turn out not to be patentable, and applicants frequently discover during the course of prosecution that only a part of what they invented and originally claimed is patentable". 191 USPQ 90, 97 (BNA) (CCPA 1976). Applicants note the features of the new claims as follows.

Claim 20

New claim 20 is drawn to a minimum promoter of mouse metallothionein I gene. None of the references cited, Bradfield '283, Waldman and Kushner '638 and O'Malley '213, teaches nor suggests a minimum promoter of metallothionein I gene.

Claim 21

New claim 21 is drawn to a minimum promoter of chicken ovalbumin gene. None of the references cited, Bradfield '283, Waldman and Kushner '638 and O'Malley '213, teaches nor suggests a minimum promoter of chicken ovalbumin gene.

Claim 22

New claim 22 is drawn to a minimum promoter of a specific nucleotide sequence of metallothionein I gene. None of the references cited, Bradfield '283, Waldman and Kushner '638

and O'Malley '213, teaches nor using such a minimum promoter. The terms newly recited in claim 22 are supported by the description at page 17, lines 16-19 of the substitute specification.

Claim 23

New claim 23 is drawn to a minimum promoter of a specific nucleotide sequence (SE ID NO: 5), derived from mouse metallothionein I gene. None of the references cited, Bradfield '283, Waldman and Kushner '638 and O'Malley '213, teaches nor suggests using such a promoter. The terms newly recited in claim 23 are supported by the description, e.g., Example 1(1), of the specification.

Claim 24

New claim 24 is drawn to a minimum promoter of a specific nucleotide sequence of chicken ovalbumin gene. None of the references cited, Bradfield '283, Waldman and Kushner '638 and O'Malley '213, teaches nor suggests using such a minimum promoter. The terms newly cited in claim 24 are supported by the description e.g., page 17, lines 19-21, of the substitute specification.

Claim 25

New claim 25 is drawn to an animal cell, in which the expression amount of the reporter gene (a) in the presence of a ligand of the ligand-responsive transcription control factor is 5-fold or more of the expression amount of the reporter gene (a) in the absence of said ligand. None of the references cited, Bradfield '283, Waldman and Kushner '638 and O'Malley '213, teaches nor

suggests such a cell. The terms newly cited in claim 25 are supported by the description e.g., page 33, line 27 to page 34, line 1, of the substitute specification.

Claim 26

New claim 26 is drawn to an animal cell, in which the expression amount of the reporter gene (a) in the presence of a ligand of the ligand-responsive transcription control factor is 10-fold or more of the expression amount of the reporter gene (a) in the absence of said ligand. None of the references cited, Bradfield '283, Waldman and Kushner '638 and O'Malley '213, teaches nor suggests such a cell. The terms newly cited in claim 26 are supported by the description e.g., page 31, lines 4-7, of the substitute specification.

Claim 27

New claim 27 is drawn to a method for obtaining an animal cell, in which the expression amount of the reporter gene (a) in the presence of a ligand of the ligand-responsive transcription control factor is 5-fold or more of the expression amount of the reporter gene (a) in the absence of said ligand. None of the references cited, Bradfield '283, Waldman and Kushner '638 and O'Malley '213, teaches nor suggests such a cell. The terms newly cited in claim 27 are supported by the description e.g., page 33, line 27 to page 34, line 1, of the substitute specification.

Claim 28

New claim 28 is drawn to a method of obtaining an animal cell, in which the expression

amount of the reporter gene (a) in the presence of a ligand of the ligand-responsive transcription control factor is 10-fold or more of the expression amount of the reporter gene (a) in the absence of said ligand. None of the references cited, Bradfield '283, Waldman and Kushner '638 and O'Malley '213, teaches nor suggests such a cell. The terms newly cited in claim 28 are supported by the description e.g., page 31, lines 4-7, of the substitute specification.

In summary, Applicants respectfully maintain that there exists no *prima facie* case of obviousness. Accordingly, the Examiner is requested to withdraw all rejections and allow the currently pending claims.

Applicants also submit that claims 20-29 as added herein are patentably distinct from the cited combinations of references.

Conclusion

A full and complete response has been made to all issues as cited in the Office Action. Applicants have taken substantial steps in efforts to advance prosecution of the present application. Thus, Applicants respectfully request that a timely Notice of Allowance issue for the present case.

If there are any minor matters precluding allowance of the application which may be resolved by a telephone discussion, the Examiner is respectfully requested to contact Craig A. McRobbie (Reg. No. 42,874) at (703) 205-8000.

Application No. 09/550,173

Docket No.: 2185-0424P

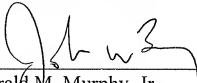
Art Unit 1636

Reply to Office Action of April 7, 2006

If necessary, the Commissioner is hereby authorized in this, concurrent, and further replies, to charge payment or credit any overpayment to Deposit Account No. 02-2448 for any additional fees required under 37 C.F.R. § 1.16 or under 37 C.F.R. § 1.17; particularly, extension of time fees.

Dated: **October 10, 2006**
(Tuesday, after a Federal Holiday)

Respectfully submitted,

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